REMARKS

Applicants wish to thank Examiner Allen for the courtesy extended to their representative, Nancy W. Vensko, on January 22, 2001, in U.S. Pat. Appl. No. 08/428,242, filed Sept 18, 1995. The Interview Summary Form PTOL-413 summarizes the discussions held at the personal interview (attached). The present remarks address the substance of the Examiner Interview.

I.   Disposition Of Claims

Claims 1-16 are presented for examination.

II.   Human and Rat Serotonin Receptor Protein St-B17

The invention relates to isolated human serotonin receptor protein St-B17 (Claim 1) and isolated rat serotonin receptor protein St-B17 (Claim 9), and related constructs, polynucleotides, cell lines, and products-by-process.

III. No New Sequence Listing

While disagreeing with the position by the PTO that depositing a biological material after the priority date introduces new matter into this application, to advance prosecution Applicant has refrained from introducing a biological deposit or deposit information herein. Neither has Applicant introduced a new sequence listing in paper form or computer readable form (CRF) into this application to conform to any biological deposit. Rather, Applicant has copied the *original* sequence listing in paper form and computer readable form (CRF) that was filed in response to the Notice to Comply in the parent application to which this continuation application relates back.

IV.   Corrected Rat and Human Sequences

Under 37 CFR 1.56, Applicant wishes to meet his duty to disclose by making of record errors in the sequence listing.

Beginning with rat, SEQ ID NO:7 is the DNA sequence and SEQ ID NO:8 is the amino acid sequence encoding rat serotonin receptor protein St-B17, as originally filed on October 26, 1992. The inventors and their colleagues subsequently published this

sequence as Monsma et al., Molecular Pharmacology 43:320 (March 1993) (attached).
Other colleagues published this sequence as Ruat et al., Biochem Biophys Res Comm
193:268 (May 1993) (attached). Later, the inventors and their colleagues published the
corrected sequence in Kohen et al., J. of Neurochemistry 66:47 (1996) (attached),
which points out the particular changes in both the DNA and amino acid sequences.

Turning to human, SEQ ID NO:12 is the DNA sequence and SEQ ID NO:13 is
the amino acid sequence encoding human serotonin receptor protein St-B17, as
originally filed on October 26, 1993. The inventors and colleagues subsequently
published the corrected sequence in Kohen et al., supra. Exhibit 1 (attached) points out
the particular changes in the DNA sequence, and Exhibit 2 (attached) points out the
particular changes in the amino acid sequence.

V.   Claiming by Crucial Third and Sixth Transmembrane Domains

The claims are directed to isolated human serotonin receptor protein St-B17
(Claim 1) and isolated rat serotonin receptor protein St-B17 (Claim 9), and related
constructs, polynucleotides, cell lines, and products-by-process, where the serotonin
receptor protein St-B17 is defined by reference to crucial transmembrane domains III
and VI. Trends in Pharmacology 13:160 (April 1992) (attached) shows that, at the time
of the Oct 26, 1992 priority date of the present application, most serotonin receptors
were known to be G protein-linked receptors having a putative seven transmembrane
domain structure. Here is Trends in Pharmacology Figure 3 showing putative
transmembrane domains numbered I to VII for previously known serotonin receptors:

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                        I                                    II
5-HT₁ββ (mouse) (48) -VALLALITLATTTLSNAFVIATVYRTRKLHTPANYLIASLAVTDLLVSILVMPISTMYTVT
5-HT₁D₁ (dog)   (41) -ALLLSIITMATALSNAFVLTTIFLTRKLHTPANYLIGSLAMTDLLVSILVMPISIAYTTT
5-HT₁D₁ (human) (41) -AVVLSVITLATVLSNAFVLTTILLTRELHTPANYLIGSLATTDLLVSILVMPISIAYTIT
5-HT₁A (rat)    (39) -SLLLGTLIFCAVLGNACVVAAIALERSLQNVANYLIGSLAVTDLMVSVLVLPMAALYQVL
5-HT₆ᵣₒ2A      (229) -SVLLGLMILVTIIGNVFVIAAIILERNLQNVANYLVASLAVADLFVACLVMPLGAVYEIS
5-HT₆ᵣₒ2B       (80) -AVVLGLMILVTIIGNVFVIAAIILERNLQNVANYLVASLAVADLFVACLVMPLGAVYEIS
5-HT₆ᵣₒ1       (165) -SIVLLIVILGTVVGNVLVCIAVCMVRFLFRPCNYLVSLALSDLCVALLVMPMALLYEVL
5-HT₁C (rat)    (57) -ALSIVVIIIMTIGGNILVIMAVSMEKFLHNATNYFLMSLAIADMLVGLLVMPLSLLAILY
5-HT₂ (rat)     (77) -ALLTTVIILTIAGNILVIMAVSLEKFLQNATNYFLMSLAIADMLLGFLVMPVSMLTILY
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The patent specification (at Example 1, page 8, line 30 et seq.) shows that, beginning with sequences that were derived from the third and sixth transmembrane domains of previously known G protein-linked receptors, the present inventors cloned and expressed a rat cDNA that encoded a novel serotonin receptor called St-B17 with high affinity for tricyclic psychotropic drugs. The pat spec (at page 12, line 15 et seq.) additionally shows that hydropathy analysis of the deduced amino acid sequence indicated seven hydrophobic regions predicted to represent putative transmembrane domains I-VII. The pat spec (at page 12, line 22 et seq.) further shows that when compared with previously known G protein-coupled receptors, the transmembrane domains of St-B17 exhibited homologies of 41%, 40%, 39%, 38%, 37%, and 36% to 5-HT2, 5-HT1D, 5-HT1C, 5-HT1B, 5-HT1A, and 5-HT1E serotonin receptors, respectively.

As indicated in Kohen et al., supra, a frame shift error had occurred in the rat clone, but the error occurred in the long carboxyl terminus tail, well past the seven transmembrane domains. As shown in Exhibits 1 and 2, a frame shift error had occurred in the human clone, too, but the error occurred in the long carboxyl terminus tail, well past the seven transmembrane domains, also. Monsma et al., supra, Figure 1, and Ruat et al., supra, Figure 1 for rat, and Kohen et al., supra, Figures 1 and 2 for human, illustrate the seven transmembrane domains. Trends in Pharmacology, supra, shows that, at the time of the Oct 26, 1992 priority date of the present application, transmembrane domain III and VI were known to contain conserved amino acids that were presumed to interact with the ligand, serotonin. Consistent with this information and the pat spec (at page 8, lines 31-34), the invention is claimed by reference to crucial transmembrane domains III and VI, the sequence from which was derived the degenerate primers to clone the rat cDNA encoding the novel serotonin receptor called St-B17.

VI.   <u>Monsma et al., Ruat et al., and Kohen et al.</u>

As indicated above, the inventors cloned and expressed a novel serotonin receptor. There is no identity with other serotonin receptors as shown by the fact that the transmembrane domains of St-B17 exhibited homologies of 41%, 40%, 39%, 38%, 37%, and 36% to 5-HT2, 5-HT1D, 5-HT1C, 5-HT1B, 5-HT1A, and 5-HT1E serotonin receptors, respectively (see supra). Additionally, the above dates show that Monsma et al. and Ruat et al., describing the cloning of the rat St-B17 serotonin receptor, occurred at a time *after* the Oct 26, 1992 priority date of the present application in which the cloning of the rat St-B17 serotonin receptor is disclosed. Furthermore, the above dates show that Kohen et al., describing the cloning of the human St-B17 serotonin receptor, occurred at a time *after* the Oct 26, 1993 priority date of the present application in which the cloning of the human St-B17 serotonin receptor is disclosed. Because these scientific publications are not *prior* art, they cannot bar patentability of the present invention.

<u>Conclusion</u>

In view of the foregoing, Applicant respectfully requests that the present amendment be entered prior to examination of this application. It is respectfully submitted that the present application is in condition for allowance. Should any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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Exhibit 1

Martinez/Needleman-Wunsch DNA Alignment
Minimum Match: 9; Gap Penalty: 1.10; Gap Length Penalty: 0.33

	Seq1(1>1984)	Seq2(1>1647)	Similarity	Gap Number	Gap Length	Consensus Length
	h5-HT6 GSDB S40337 flatfile	Seq ID 12 h5-HT6 Index				
	(333>1984)	(1>1647)	97.2	16	17	1658
	(333>1984)	(1>1647)	97.2	16	17	1658

(handwritten: accession No for genbank)

(handwritten: 12 = human STB-17)

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          v340      v350      v360      v370      v380      v390      v400      v410
ACTCACCTCCCCCGGGGGGGCGTGGTGAGTCGGCGGTCGCGGTCGTGTTCTCACGGACGGTCCCCGTCCCAGCCTGCCTTCGCCGGGGGC
ACTCACCTCCCCCGGGGGGGCGTGGTGAGTCGGCGGTCGCGGTCGTGTTCTCACG ACGGTCCCCGTCCCAGCCTGCCTTCGCCGGGGGC
ACTCACCTCCCCCGGGGGGGCGTGGTGAGTCGGCGGTCGCGGTCGTGTTCTCACG-ACGGTCCCCGTCCCAGCCTGCCTTCGCCGGGGGC
 ^10       ^20       ^30       ^40       ^50       ^60       ^70

          v420      v430      v440      v450      v460      v470      v480      v490
CCTCATCTGCTTTCCCGCCACCCTATCACTCCCTTGCCGTCCACCCTCGGTCCTCATGGTCCCAGAGCCGGCCCAAACCG
CCTCATCTGCTTTCCCGCCACCCTATCACTCCCTTGCCGTCCACCCTCGGTCCTCATGGTCCCAGAGCCGGCCCAACCG
CCTCATCTGCTTTCCCGCCACCCTATCACTCCCTTGCCGTCCACCCTCGGTCCTCA TGGTCCCAGAGCCGGGCCCAACCG
 ^80       ^90       ^100      ^110      ^120      ^130      ^140      ^150
                                                           start

          v500      v510      v520      v530      v540      v550      v560      v570
CCAATAGCACCCCGGCCTGGGGGGGCAGGCCGCC-GTCGG     GGGGGGCAGCGGCTGGCGGCCCGCG-CTGTGCG
CCAATAGCACCCCGGCCTGGGGGGGCAGGCCGCC-GTCGG    GGGGGGCAGCGGCTGGCGGCCCGCG  G CTGTGCG
CCAATAGCACCCCGGCCTGGGGGGGCAGGCAGG C GCC GTCG GGGGGGCAGCGGCTGGCGGCCCG G CTGTGCG
CCAATAGCACCCCGGCCTGGGGGGGCAGG-C-GCCCGTCGNNN--GGGGGGCAGCGGCTGGCGGCCCG-GCCTGTGCG
 ^160      ^170      ^180      ^190      ^200      ^210      ^220      ^230

          v580      v590      v600      v610      v620      v630      v640      v650
TGGTCATCGCGCTGACGCGGCGGCCAACTCGCTGCTGATCGGCTCATCGCCGGCTGCGCAACACGTCC
TGGTCATCGCGCTGACGCGGCGGCCAACTCGCTGCTGATCGGCTCATCGCCGGCTGCGCAACACGTCC
TGGTCATCGCGCTGACGCGGCGGCCAACTCGCTGCTGATCGGCTCATCGCCGGCTGCGCAACACGTCC
 ^240      ^250      ^260      ^270      ^280      ^290      ^300      ^310

          v660      v670      v680      v690      v700      v710      v720      v730
AACTTCTTCCTGGTGTGCGCTCTTCACGTCTGACCTGATGGTGGGGCTGGTGGTGATGCCGCCGGCTGAACGCGCT
AACTTCTTCCTGGTGTGCGCTCTTCACGTCTGACCTGATGGT GGGCTGGTGGTGATGCCGCCGGCTGAACGCGCT
AACTTCTTCCTGGTGTGCGCTCTTCACGTCTGACCTGATGGTCGGGCTGGTGGTGATGCCGCCGGCTGAACGCGCT
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          ^320      ^330      ^340      ^350      ^360      ^370      ^380      ^390
              v740      v750      v760      v770      v780      v790      v800      v810

GTACGGGGCGCTGGGTGCTGGCGGCGGCGGCCTCTGCTGCCTTCGACGTGATGTGCTGCAGCGCCTCCATCC
GTACGGGGCGCTGGGTGCTGGCGGCGGCGGCCTCTGCTGCCTTCGACGTGATGTGCTGCAGCGCCTCCATCC
GTACGGGGCGCTGGGTGCTGGCGGCGGCGGCCTCTGCTGCCTTCGACGTGATGTGCTGCAGCGCCTCCATCC
          ^400      ^410      ^420      ^430      ^440      ^450      ^460      ^470

          ^400      ^410      ^420      ^430      ^440      ^450      ^460      ^470
              v820      v830      v840      v850      v860      v870      v880      v890

TCAACCTCTGCCTCATCAGCCTGGACCGCTACCTGCTCATCCTCGCCCGCTACAAGCTGCGCATGACGCCCCTG
TCAACCTCTGCCTCATCAGCCTGGACCGCTACCTGCTCATCCTCGCCCGCTACAAGCTGCGCATGACGCCCCTG
TCAACCTCTGCCTCATCAGCCTGGACCGCTACCTGCTCATCCTCGCCCGCTACAAGCTGCGCATGACGCCCCTG
          ^480      ^490      ^500      ^510      ^520      ^530      ^540      ^550

          ^480      ^490      ^500      ^510      ^520      ^530      ^540      ^550
              v900      v910      v920      v930      v940      v950      v960      v970

CGTGCCCCTGGCCCTAGTCCTGGGCGCCTGGAGCCTCCTGCCCTGCTCCTGCCCTGCTGGGCTGGCACGA
CGTGCCCCTGGCCCTAGTCCTGGGCG CTGGAGCCTCCTGCCCTGCTCCTGCCCTGCTGGGCTGGCACGA
CGTGCCCCTGGCCCTAGTCCTGGGCGCTGGAGCCTCCTGCCCTGCTCCTGCCCTGCTGGGCTGGCACGA
          ^560      ^570      ^580      ^590      ^600      ^610      ^620      ^630

          ^560      ^570      ^580      ^590      ^600      ^610      ^620      ^630
              v980      v990      v1000     v1010     v1020     v1030     v1040     v1050

GCTGGGCCACGCGGCCACGGCCACCCGTCCCTGGCCAGTGCCCGTCCTTTGTCCTTGTGGCGTCGGGCC
GCTGGGCCACGCACGGCCACCCGTCCCTGGCCAGTGCCCGTCCTTTGTCCTTGTGGCGTCGGGCC
GCTGGGCCACGCACGGCCACCCGTCCCTGGCCAGTGCCCGTCCTTTGTCCTTTGTGGCGTCGGGCC
          ^640      ^650      ^660      ^670      ^680      ^690      ^700      ^710

          ^640      ^650      ^660      ^670      ^680      ^690      ^700      ^710
              v1060     v1070     v1080     v1090     v1100     v1110     v1120     v1130

TCACCTTCTTCCTGCCCCTCGGGTGCCATATGCTTCACCTACTGCAGGATCCTGCTAGCTGCCCGGCAAGCAGGCCGTGCAG
TCACCTTCTTCCTGCCCCTCGGGTGCCATATGCTTCACCTACTGCAGGATCCTGCTAGCTGCCCGGCAAGCAGGCCGTGCAG
TCACCTTCTTCCTGCCCCTCGGGTGCCATATGCTTCACCTACTGCAGGATCCTGCTAGCTGCCCGGCAAGCAGGCCGTGCAG
          ^720      ^730      ^740      ^750      ^760      ^770      ^780      ^790

          ^720      ^730      ^740      ^750      ^760      ^770      ^780      ^790
              v1140     v1150     v1160     v1170     v1180     v1190     v1200

GTGGCCTCCCTCACCACCGGCATGGCCAGTCAGGCCTCGGAGACGCTGCAGGTGCCCGAGACCCCACGCC-CAGGGGTGG
GTGGCCTCCCTCACCACCGGCATGGCCAGTCAGGCCTCGGAGACGCTGCAGGT CCCAGA GC  CAGGGGTGG
GTGGCCTCCCTCACCACCGGCATGGCCAGTCAGGCCTCGGAGACGCTGCAGGTACCCAGGAGCCCA-GCGGGCAGGGGTGG
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          ^800      ^810      ^820      ^830      ^840      ^850      ^860      ^870

v1210     v1220     v1230     v1240     v1250     v1260     v1270     v1280
AGTCTGCTGACAGCAGGCGGTCTAGCCACGAGGAAGCA-CAGCAGGAGGCCTGAAGGCCAGCCTGACGCTGGGCATCCTGCT
AGTCTGCTGACAGCAGGCGGTCTAGC ACGAAG A CAGCAGGAAGG CCTGAAGGCCAGC TGACGCTGGGCATCCTGCT
AGTCTGCTGACAGCAGGCGGTCTAGCAACGAAG-AGCAGCAGGAAGGGCCTGAAGGCCTGAAGGCCAGCATGACGCTGGGCATCCTGCT
          ^880      ^890      ^900      ^910      ^920      ^930      ^940      ^950

v1290     v1300     v1310     v1320     v1330     v1340     v1350     v1360
GGGCATGTTCTTTGTGACCTGGTTGCCCTTCTTTGTGGCCAACATAGTCCAGGCCGTGTGCGACTGCATCTCCCCAGGCC
GGGCATGTTCTTTTGTGACCTGGTTGCCCTTCTTTGTGGCCAACATAGTCCAGGCCGTGTGCGACTGCATCTCCCCAGGCC
GGGCATGTTCTTTGTGACCTGGTTGCCCTTCTTTGTGGCCAACATAGTCCAGGCCGTGTGCGACTGCATCTCCCCAGGCC
          ^960      ^970      ^980      ^990      ^1000     ^1010     ^1020     ^1030

v1370     v1380     v1390     v1400     v1410     v1420     v1430     v1440
TCTTCGATGTCCTCACATGGCTGGGTTACTGTAACAGCACCATGAACCCCATCATCTACCCACTCTTCATGCGGGGACTTC
TCTTCGATGTCCTCACATGGCTGGGTTACTGTAACAGCACCATGAACCCCATCATCTACCCACTCTTCATGC GGACTTC
TCTTCGATGTCCTCACATGGCTGGGTTACTGTAACAGCACCATGAACCCCATCATCTACCCACTCTTCATGCTTGGACTTC
          ^1040     ^1050     ^1060     ^1070     ^1080     ^1090     ^1100     ^1110

v1450     v1460     v1470     v1480     v1490     v1500     v1510     v1520
AAGCGGGGCGCTGGGCAGGTTCCTGCCATGTCCACGCTGTCCCCGGGAGCGCCAGGCCAGGCCTGCCATCACTGCG
AAGCGGGGCGCTGGGCAGGTTCCTGCCATGTCCACGCTGTCCCCGGGAGC CCAGGCCAGCCTGCCATCACTGCG
AAGCGGGGCGCTGGGCAGGTTCCTGCCATGTCCACGCTGTCCCCGGGAGC-CCAGGCCAGCCTGCCATCACTGCG
          ^1120     ^1130     ^1140     ^1150     ^1160     ^1170     ^1180     ^1190

v1530     v1540     v1550     v1560     v1570     v1580     v1590     v1600
CACCTCTCACAGCGGCCCCGGGCCCCGGCCCTTAGCCTACAGCAGGTGCTGCCGCCCTGCCGCGCCCTGCCGACTCAGATTCGG
CACCTCTCACAGCGGCCCCGGGCCCCGGCCCTTAGCCTACAGCAGGTGCTGCCGCCCTGCCGCGCCCTGCCGACTCAGATTCGG
CACCTCTCACAGCGGCCCCGGGCCCCGGCCCTTAGCCTACAGCAGGTGCTGCCGCCCTGCCGCGCCCTGCCGACTCAGATTCGG
          ^1200     ^1210     ^1220     ^1230     ^1240     ^1250     ^1260     ^1270

v1610     v1620     v1630     v1640     v1650     v1660     v1670     v1680
ACTCAGACGCAGCTCAGGCGGCTCCTCGGGCCTCGGGCTGCGGCTCACGGCCCAGCTGCTTCCTGGCGGAGGCCACCCAGGAC
ACTCAGACGCAGCTCAGGCGGCTCCTCGGGCCTCGGGC TGCGGCTCACGGCCCAGCTGCTTCCTGGCGGAGGCCACCCAGGAC
ACTCAGACGCAGCTCAGGCGGCTCCTCGGGCCTCGGGCGTGCGGCTCACGGCCCAGCTGCTTCCTGGCGGAGGCCACCCAGGAC
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               ^1280        ^1290        ^1300        ^1310        ^1320        ^1330        ^1340        ^1350
v1690    , v1700        v1710        v1720        v1730        v1740        v1750        v1760
CCCCGCTGCCCACCAGGGCCGCGCTGCCGCCGTCAATTTCTTCAACATCG-ACCCCGCGGAGAGCCCGAGCTGCGGCCGCATC
CCCCGCTGCCCACCAGGGCCGCGCTGCCGCCGTCAATTTCTTCAACATCG ACCCCGCGGAGAGCCCGAGCTGCGGCCGCATC
CCCCGCTGCCCACCAGGGCCGCGCTGCCGCCGTCAATTTCTTCAACATCGSACCCCGCGGAGAGCCCGAGCTGCGGCCGCATC
               ^1360        ^1370        ^1380        ^1390        ^1400        ^1410        ^1420        ^1430

v1770        v1780        v1790        v1800        v1810        v1820        v1830        v1840
CACTTGGCATCCCCACGAACTGACCCGGGCTTGGGGCTGGCCAATGGGGAGCTGGATTGAGCAGAACCCAGACCCTGAGT
CACTTGGCATCCCCACGAACTGACCC GGCTTGGGGCTGGCCAATGGGGAGCTGGATTGAGCAGAACCCAGACCCTGAGT
CACTTGGCATCCCCACGAACTGACCC-GGCTTGGGGCTGGCCAATGGGGAGCTGGATTGAGCAGAACCCAGACCCTGAGT
               ^1440        ^1450        ^1460        ^1470        ^1480        ^1490        ^1500        ^1510

v1850        v1860        v1870        v1880        v1890        v1900        v1910        v1920
CCTTGGGCCAGCTCTTGGCTAAGACCAGGAGGCTGCAAGTCTCCTAGAAGCCCTCTGAGCTCCAGAGGGGTGCG-CAGAG
CCTTGGGCCAGCTCTTGGCTAAGACCAGGAGGCTGCAAGTCTCCTAGAAGCCCTCTGAGCTCCAGAGGGGTGCG CAGAG
CCTTGGGCCAGCTCTTGGCTAAGACCAGGAGGCTGCAAGTCTCCTAGAAGCCCTCTGAGCTCCAGAGGGGTGCGGCAGAG
               ^1520        ^1530        ^1540        ^1550        ^1560        ^1570        ^1580        ^1590

v1930        v1940        v1950        v1960        v1970        v1980
CTGACCCCCTGCTGCCATCTCCAGGCCCCTTACCTGCAGGGATCATAGCTGACTCAGA
CTGACCCCCTGCTGCCATCTCCAGGCCCCTTACCTGCAGGGATCATAGCTGACT AGA
CTGACCCCCTGCTGCCATCTCCAGGCCCCTTACCTGCAGGGATCATAGCTGACT-AGA
               ^1600        ^1610        ^1620        ^1630        ^1640
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Exhibit 2

Lipman-Pearson Protein Alignment

Seq1(1>440)	pep h5-HT6 GSDB S40337 Flatfile PEP	(1>440)			
Seq2(1>439)	Seq ID 13 - h 5-HT6 from application	(1>439)			

Similarity Index	Gap Number	Gap Length	Consensus Length
79.6	5	5	442

Consensus →

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            v10       v20       v30       v40       v50       v60       v70       v80       v90       v100      v110      v120
   MVPEPGPTANSTPAWGAGPPSAPGGSGWVAAALCVVIALTAAANSLLIALICTQPALRNTSNFFLVSLFTSDLMVGLVVMPPAMLNALYGRWVLARGLCLLWTAFDVMCCSASILNLCLI
   |||||||||||||||||||||||::...:||||||||:||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 → MVPEPGPTANSTPAWGAGARXX-GGSGWVAAGLCVVIALTAAANSLLIALICTQPALRNTSNFFLVSLFTSDLMVGLVVMPPAMLNALYGRWVLARGLCLLWTAFDVMCCSASILNLC
   ^10       ^20       ^30       ^40       ^50       ^60       ^70       ^80       ^90       ^100      ^110

            v130      v140      v150      v160      v170      v180      v190      v200      v210      v220      v230      v240
   SLDRYLLILSPLRYKLRMTPLRALALVLGAWSLAALASFLPLLLGWHELGHARPPVPGQCRLLASLPFVLVASGLTFFLPSGAICFTYCRILLAARKQAVQVASLTTGMASQASETLQVP
   |||||||||||||||||||||||||||:.:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
   SLDRYLLILSPLRYKLRMTPLRALALVLGGWSLAALASFLPLLLGWHELGHARPPVPGQCRLLASLPFVLVASGLTFFLPSGAICFTYCRILLAARKQAVQVASLTTGMASQASETLQVP
   ^130      ^140      ^150      ^160      ^170      ^180      ^190      ^200      ^210      ^220      ^230

            v250      v260      v270      v280      v290      v300      v310      v320      v330      v340      v350      v360
   RTPRPGVESADSRRLATKHSRKALKASLTLGILLGMFFVTWLPFFVANIVQAVCDCISPGLFDVLTWLGYCNSTMNPIIYPLFMRDFKRALGRFLPCPRCPRERQASLASPSLRTSHSGP
   |:| :|||||||||||||| ||:||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||:: .:|:.  .: ::|
   RSPAAGVESADSRRLATKSSRKGLKASMTLGILLGMFFVTWLPFFVANIVQAVCDCISPGLFDVLTWLGYCNSTMNPIIYPLFMLDFKRALGRFLPCPRCPREPRPAWFRHHCAPLTAAP
   ^250      ^260      ^270      ^280      ^290      ^300      ^310      ^320      ^330      ^340      ^350

            v370      v380      v390      v400      v410      v420      v430      v440
   RPGLSLQQVLPLP-LPPDSDSDAGSGG-SSGLRLTAQLLLFGEATQDPPLPTRAAAAVNFFNIDPAEPELRPHPLGIPTN
   |:|.:  .  :.::|: .|| .|: | :| . .|..|. | .:::::. . ||||||||||||||||||||
   GPALAYSRCCRCPCRRTQIRTGTQAQAAPRACGSRPSCCFLARPPRTPPCP-PGPLPESIGS-TSKPAEPELRPHPLGIPTN
   ^360      ^370      ^380      ^390      ^400      ^410      ^420      ^430
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